Stilbene a new antibiotic class for topical and systemic administration

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Mucosinix Pharm
This is a Unique and Critical Time for Antibiotic Drug Development

- Overcrowding and overburdening of hospitals due to the COVID-19 pandemic
  - Reuse of PPE and sharing of ventilators due to limited resources
  - Poorer compliance for reporting antibiotic use and infection rates
  - Anecdotal surging antibiotic use to treat COVID-19
- Result is a climate encouraging the spread of multi-drug resistant organisms
- Viral illnesses increase susceptibility for secondary bacterial infections (secondary bacterial pneumonia has historically been a notable cause of death during viral pandemics)
- DISARM Act of 2019 introduced to the House (Subcommittee on Health)
  - Proposes increasing hospital reimbursement for antibiotics, and incentivizing development of robust effective antimicrobial stewardship programs
- NOW IS THE TIME TO ACT!
Antibiotic classes are limited and drug resistance is climbing.

Antibiotic resistance is a major health crisis.

Ribosome inhibitors; cell wall inhibitors.
Photorhabdus EVOLVED antimicrobials to protect their food source

Mutualism

Bacteria colonize the gut of nematode worms

Pathogenesis

Nematode infects insect and releases bacteria

Nematodes and bacteria reproduce

Bacteria multiply and kill the insect

Bacteria and nematodes search for another meal

P. asymbiotica infects humans

Tapinarof


Stilbenes are polyketides widely distributed in dietary plants.

**Plant Stilbene Diversification**

- **Isomerization**
- **Glycosylation**
- **Isoprenylation**
- **Methylation**
- **Oligomerization**

**Bacterial stilbene (substrate)**

- **Tapinarof**

- Clinical efficacy for psoriasis & atopic dermatitis (GSK)
- Activates AhR (nm) and Nrf2 to promote clinical efficacy

Stilbene supplements can alleviate IBD symptoms
Duotap: A Novel Antibiotic with a New Indication

Antibiotic market for MRSA antibiotics (1.3 billion market by 2026)

MUX-001 Drug Lead ("Duotap")

Using evolution as a guide, we discovered MUX-001, a novel stilbene drug lead for MRSA

GSK recently sold Tapinarof to Dermavant Sciences for $330 million.
Duotap is effective against drug resistant bacteria

MUX-001
Drug Lead
(Duotap)

- New class effective against multidrug resistant organisms (Cell wall biosynthesis inhibitor)
- MRSA does not develop resistance to MUX-001
Duotap inhibits cell wall biosynthesis

Tyler Goddard & Hyun Bong Park

Image: Hancock, L.E., Murray, B.E., Sillanpaa, J. Enterococcal Cell Wall Components and Structures.
Funded Animal Study

- Efficacy Assessment in Murine MRSA Dermal Infection Model
- Contracted through TransPharm Preclinical Solutions
- Funding already secured through YCCI Research Support Award
  - Female, SKH-1 hairless mice ordered from Charles River
  - Targeted challenge inoculate of 6.0 log10 CFU organisms per 100 μL Methicillin resistant Staphylococcus aureus
  - Test articles will be administered topically at 4, 8 and 12 hours
  - Efficacy of test articles will be determined by comparison of CFU per gram of tissue between the vehicle group and test article groups
- Results in progress
IP: Provisional patent filed for compositions of matter and methods of use.

- Biocatalytic pipeline to generate Mux analogs (new compositions of matter)
- Use as an anti-infective against MDR pathogens (provisional in place)

2-year proposal: $100K (Phase 1)

- Phase 1
  - Topical dose ranging study $30,000
  - Oral and intraperitoneal PK study $30,000
  - Pan laboratories liver microsome study and P450 preliminary tox study $40,000

- Phase 2
  - Medicinal chemistry program with Jubilant for oral bioavailability $200,000